REMARKS/ARGUMENTS

Claims 1 and 2 have been amended. Claims 13 to 29 are newly added.

Support for new claim 13 can be found as follows. Support for the term "isolated" can be found, for example, on page 15, line 30 of the disclosure as filed. Support for the expression "post-natal" can be found, for example, in original claim 1. Support for the expression "pancreatic islet cells" can be found, for example, on page 15, line 30 of the disclosure as filed.

Support for the expression "95% pure" found in new claim 14 can be found, for example, on page 15, line 31 of the disclosure as filed.

Support for the expression "100% transformed" found in new claim 15 can be found, for example, on page 15, lines 31-32 of the disclosure as filed.

Support for new claim 16 can be found as follows. Support for the expression "CK-19 duct epithelial cell marker" can be found, for example, on page 17, lines 3-4 of the disclosure as filed. Support for the expression "insulin-less" can be found, for example, on page 14, lines 19-21 of the disclosure as filed.

Support for the expression "appearance of solid spherical structures" found in new claim 17 can be found, for example, on page 14, lines 32-33 of the disclosure as filed.

Support for the expression "appearance of endosecretory granules" found in new claim 18 can be found, for example, on page 14, lines 34-35 of the disclosure as filed.

Support for the expression "increase in expression of the pro-insulin mRNA" found in new claim 19 can be found, for example, on page 14, line 35 and page 15, line 1, of the disclosure as filed.

Support for the expression "increase in expression of PDX-1" found in new claim 20 can be found, for example, on page 16, lines 15-16 of the disclosure as filed.

Support for the expression "increase in the percentage of differentiated islet cells" found in new claim 21 can be found, for example, on page 16, lines 28-33 of the disclosure as filed.

Support for the expression "increase in expression of an islet cell hormone" found in new claim 22 can be found, for example, on page 17, lines 10-16 of the disclosure as filed.

Support for the expression "increase in insulin secretion" found in new claim 23 can be found, for example, on page 17, lines 17-24 of the disclosure as filed.

Support for the expression "increase in cell survival" found in new claim 24 can be found, for example, on page 18, lines 7-12 of the disclosure as filed.

Support for new claim 25 is identical to the support listed above for claims 17 to 24.

Support for new claims 26 to 29 for the islet cell hormones "insulin", "glucagon" and "somatostatin" can be found, for example, on page 17, lines 10-16 of the disclosure as filed.

Rejections under 35 U.S.C. § 102

The Examiner has rejected former claims 1 to 4 under 35 U.S.C. § 102(a) as being anticipated by Roberts. This rejection has been considered and reconsideration is respectfully requested on the following grounds.

First, the claims have been amended to be restricted to a dedifferentiated population of duct epithelial cells with at least bipotentiality. Support for the term "dedifferentiated" can be found, for example, in original claim 2. Support for the expression "population of duct epithelial cells" can be found, for example, on page 16, lines 11-12 of the disclosure as filed. Support for the expression "with at least bipotentiality" can be found, for example, in original claim 2.

Second, the cells of Roberts are of fetal origin, while the cells of the present invention are of adult (post-natal) origin. The cells of Roberts are referred to as "pancreatic progenitor cells" that may become exocrine and endocrine cells. These cells are in a

pre-differentiated state and are therefore different from dedifferentiated duct epithelial cells. The cell types as known from Robert are not dedifferentiated but undifferentiated and are thus different from the cells of the present invention.

Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Rejections under 35 U.S.C. § 103

The Examiner has rejected former claims 1 to 4 under 35 U.S.C. § 103(a) as being unpatentable over the combination of each of Korsgren and Oberg-Welsh in view of Bonner-Weir. This rejection has been considered and reconsideration is respectfully requested on the following grounds.

First, the claims have been amended to be restricted to a dedifferentiated population of duct epithelial cells with at least bipotentiality. The cells of either of Korsgren or Oberg-Welsh are of fetal origin, while the cells of the present invention are of adult (post-natal) origin. Again, these cells are in a pre-differentiated state and are therefore different from the dedifferentiated duct epithelial cells of the present invention. The usefulness and reliability of the cells of Korsgren or Oberg-Welsh in transdifferentiation is completely unknown and it cannot be expected that the method of the invention would reliably function using such cell population.

Second, the method taught by Bonner-Weir includes a selection step for differentiated ductal cells, which are therefore not dedifferentiated cell. Importantly, this cell culture selection step for differentiated ductal cells involves deliberately discarding the islet cells at the basis of the present invention. Hence, the method taught by Bonner-Weir effectively teaches away from the present invention.

Third, inventiveness lies in the use of a dedifferentiate population of duct epithelial cells. It was unexpected, and therefore not obvious, to achieve dedifferentiation of a population of isolated post-natal islet cells to produce the cells of the present invention. The main advantage and, doubtless, new aspect of the present invention is to provide a method allowing to identify agents capable of inducing or re-establishing the transdifferentiation from bi- or multipotential dedifferentiated duct cells back to insulin

producing cells. The main challenge of this method was to identify the right cell population which could be transdifferentiated in both directions and could therefore be useful in a standardized screening method as claimed in the present invention. Therefore, it was not obvious to establish the concept of the screening method exploiting transdifferentiation and then select an appropriate dedifferentiated cell population.

Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner has rejected former claims 1 to 4 under 35 U.S.C. § 112, second paragraph, as being indefinite. This rejection has been considered and reconsideration is respectfully requested on the following grounds.

First, claim 1 has been amended to clarify it: the term "potency" has been replaced with the term "effectiveness".

Second, claim 1 has been further amended to clarify what is determined and to add a correlating steps. The expression "by determining a parameter indicative of insulin production" has been added. Moreover, new claims 17 to 25 have been added to further define the term "parameter". Support for these new claims is found in the disclosure as filed, as described above. No new matter has been added.

Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Objections

The Examiner objects to the abstract of the disclosure because it contains legal terminology. This objection has been considered and the abstract has been amended to remove the legal terminology.

Reconsideration and withdrawal of this objection is therefore respectfully requested.

In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

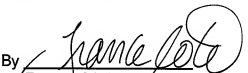
If there are any questions regarding this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned at (514) 871-2929 so that such questions can be expeditiously resolved.

FEE AUTHORIZATION

Should any fees associated with the submission be required, the Commissioner is authorized to charge such deficiencies to our Deposit Account No. 02-2095. Any overpayments should be credited to said Deposit Account.

Respectfully submitted,

Moshe Szyf et al.

By 
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